

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
23 June 2005 (23.06.2005)

PCT

(10) International Publication Number  
**WO 2005/056830 A3**

(51) International Patent Classification: **C12Q 1/68**

(21) International Application Number:  
PCT/GB2004/005033

(22) International Filing Date:  
1 December 2004 (01.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0328451.0 9 December 2003 (09.12.2003) GB

(71) Applicant (for all designated States except US): **NATIONAL BIOLOGICAL STANDARDS BOARD** [GB/GB]; National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 2QG (GB).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **HAWKINS, John, Ross** [GB/GB]; National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 2QG (GB).

(74) Agent: **I.P. 21 LIMITED**; Norwich Research Park, Colney, Norwich NR4 7UT (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

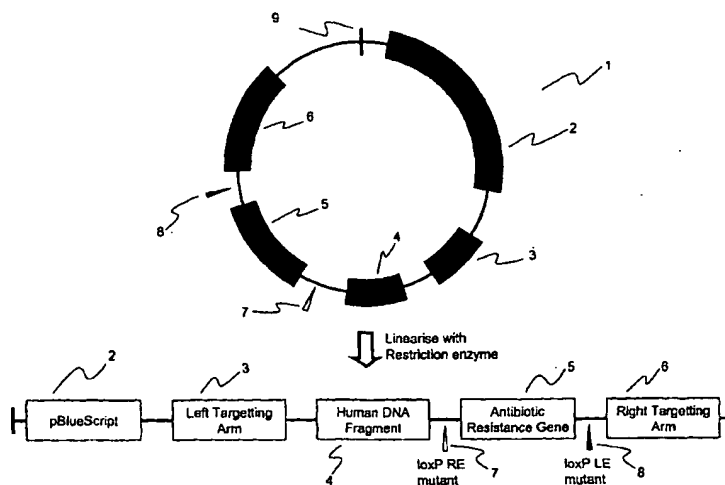
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

[Continued on next page]

(54) Title: GENETIC REFERENCE MATERIALS



(57) Abstract: The invention provides a genetic reference standard comprising at least one human genetic reference sequence (comprising a human DNA sequence containing at least one genetic variant whose presence in the DNA of a human subject is indicative of a pathological condition, a predisposition to a pathological condition, or a predisposition to an adverse reaction to external stimuli, or is indicative of a patient's likely response to a therapeutic intervention, i.e. a variant used in pharmacogenomic analysis) cloned into a non-mammalian animal cell line. There are also provided such reference standards where the human DNA is targeted to specific location in the host genome, using homologous recombination. The invention further provides a method of detecting a genetic variant using such reference standards.

BEST AVAILABLE COPY

WO 2005/056830 A3



MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

**Published:**

— with international search report

(88) Date of publication of the international search report:

9 March 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

BEST AVAILABLE COPY